

### **DETAILED ACTION**

1. The Request for Continued Examination (RCE) filed on July 2, 2009 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

#### ***Status of the Claims***

2. Claims 10-12, 15, 19-24 and 35 are pending.

Applicants' amendment filed July 2, 2009 is acknowledged. Applicants' response has been fully considered. Claim 10 has been amended, claims 25-34 have been cancelled, and a new claim 35 has been added. Therefore, claims 10-12, 15, 19-24 and 35 are examined.

#### **Withdrawn Claim Rejections - 35 USC § 112**

3. The previous rejection of claims 10-12, 15 and 19-24 under 35 U. S. C. 112, first paragraph, new matter, is withdrawn in view of applicants' amendment to the claims, and applicants' response at pages 6-7 in the amendment filed July 2, 2009.

#### ***Examiner's Amendment***

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Amanda Murphy on July 10, 2009.

#### **Examiner's Amendment to the Claims:**

Claims 10 and 15 have been amended as follows:

10. (Currently amended) A process for producing a concentrate of a factor VIII:C-containing von Willebrand factor (vWF/FVIII:C), comprising subjecting a liquid

comprising factor VIII:C (FVIII:C) and von Willebrand factor (vWF) to a fractional precipitation using an effective amount of at least one of an alkali metal salt or an alkaline earth metal salt, and an amino acid chosen from glycine,  $\alpha$ - or  $\beta$ -alanine,  $\alpha$ - or  $\beta$ - or  $\gamma$ -aminobutyric acid, lysine, valine, asparagine, and glutamic acid, wherein the fractional concentration of the amino acid is from about 67 to about 110 g/l, such that the produced concentrate has an increased content of high molecular weight multimers of vWF, and a ratio of von Willebrand factor ristocetin cofactor activity (vWF:RCof) to von Willebrand factor antigen (vWF:Ag) of greater than 1.

15. (Currently amended) The process as claimed in claim 10 further comprising:

stabilizing the concentrate product produced during said process with at least one of sucrose, glycine, calcium ions, and albumin; and

pasteurizing said concentrate product produced during said process.

**The following is an Examiner's Statement of Reasons for Allowance:** The following reference is related to the claimed invention. Heimburger *et al.* (Factor VIII Concentrate, Highly-Purified and Heated in Solution, Drug Res. 31(I), Nr. 4, 619-622 (1981); English translation of the article) teach a method to produce a highly purified factor VIII concentrate by adsorbing a pooled cryoprecipitate from citrated plasma on aluminum hydroxide, removing fibrinogen by heat denaturation in the presence of glycine; precipitating factor VIII using sodium chloride, where the ratio of VIII:RCOF activity to VIII R:Ag activity is less than 1. Bhattacharva *et al.* (U.S. Patent 5,288,853) teach a process of purifying factor VIII complex using heparin-coupled chromatography, where the factor VIII complex is eluted from the column with an aqueous solution containing  $\text{CaCl}_2$  and histidine, and the factor VIII complex is further purified by precipitation with glycine (2 M, corresponding to 150 g/l; Examples 3-7) and sodium chloride (0.83-1.93 M, corresponding to 49-113 g/l). However, either Heimburger *et al.* or Bhattacharva *et al.* do not teach a method of producing a concentrate of vWF/FVIII:C by

fractional precipitation using an effective amount of at least one of an alkali metal salt or an alkaline earth metal salt, and an amino acid chosen from glycine,  $\alpha$ - or  $\beta$ -alanine,  $\alpha$ - or  $\beta$ - or  $\gamma$ -aminobutyric acid, lysine, valine, asparagine, and glutamic acid, wherein the fractional concentration of the amino acid is from about 67 g/l (e.g., 66.7 or 71.1 g/l, "about" is considered as  $\pm 10\%$ ) to about 110 g/l (e.g., 100 or 109.6 g/l), such that the produced concentrate has an increased content of high molecular weight multimers of vWF, and a ratio of von Willebrand factor ristocetin cofactor activity (vWF:RCof) to von Willebrand factor antigen (vWF:Ag) of greater than 1. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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/Chih-Min Kam/

Primary Examiner, Art Unit 1656

CMK

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